LETTER TO THE EXAMINER		
	Application #	09/964,858
	Confirmation #	2374
	Filing Date	September 28, 2001
	First Inventor	HOSTETTER
	Art Unit	1645
	Examiner	Devi, Sarvamangala J.N.
	Docket #	P07274US02/BAS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S I R:

Further to Applicants' response to the Office Action filed on December 27, 2004, Applicants now submit the executed copy of the Declaration of Dr. Margaret D. Hostetter, Ph.D., with minor amendments to the language of the Declaration.

For reasons as set forth in the previously filed response, Applicants submit that the present application is now in condition for allowance, and such action is earnestly solicited.

Respectfully submitted,

Date: January 4, 2005

By: B. Aaron Schulman
Registration No.: 31877

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DECLARATION UNDER RULE 132		
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S I R:

I, Dr. Margaret K. Hostetter, M.D., declare and say as follows:

1. I am the first named inventor of the above identified application. I am a Professor and Chair of the Department of Pediatrics and Physician-In-Chief for Yale New Haven Children's Hospital of the Yale University School of Medicine. I have also been an inventor or co-inventor on numerous patents and articles in the field of the present invention. I am thus well familiar with the subject matter of the claims of the present application.

2. The present invention is directed to the recent discovery of the amino terminal sequence (propeptide) of the Int1p protein of *Candida albicans* and the role it plays in the activation of T lymphocytes in host cells. As is set forth in the specification of the above application, it was discovered that the amino terminal sequence (or some polypeptide therein) is a superantigen-like moiety which is cleaved from Int1p and subsequently triggers activation of human T lymphocytes and expands Vbeta subsets 2 and 14.

3. In the present application, we have discovered that antibodies that recognize the amino terminal region have the ability to inhibit the activation of T lymphocytes caused by *Candida albicans* and to prevent the expansion of Vbeta T cell subsets that occurs in response to *C. albicans* and to the superantigen-like moiety contained within the first 263 amino acids of Int1p. In particular, antibodies to the amino terminal region in accordance with the invention are capable of inhibiting the activation of T lymphocytes and preventing the expansion of Vbeta subsets in a manner not previously possible using prior antibodies to Int1p.

4. In my prior patents, including U.S. Patent No. 5,886,151 and 6,774,219 (issuing from cited U.S. Pat. App. Ser. No. 09/978,343), antibodies were disclosed which were capable of recognizing the RGD sequence at the carboxy-terminus of Int1p, and we reported that such antibodies were able to block adhesion of *C. albicans* to host cells. However, the fact that the prior antibodies could block adhesion has nothing to do with the ability to inhibit T lymphocyte activation and prevent the expansion of Vbeta subsets. Accordingly, because the prior antibodies were **not** directed to the amino terminal region containing the superantigen moiety they did **not** exhibit the properties of the antibodies of the present invention, namely inhibiting the activation of T lymphocytes and preventing the expansion of Vbeta subsets 2 and 14. My prior patents thus do not disclose or suggest antibodies to the amino terminal region which unexpectedly have the ability to inhibit activation of T lymphocytes and prevent expansion of Vbeta subsets.

5. Further, our laboratory has performed additional tests of the ability of the antibodies in accordance with the present invention to bind to the amino terminal

region so as to prevent the formation of cleaved superantigen and prevent T lymphocyte activity. In these tests, two different antibodies capable of binding to the amino terminal region, identified as "MAb 163.5" and "MAb 253.4", were introduced at various dosages, and the inhibition of T lymphocyte was monitored in each case. The table that follows below represents the percentage of inhibition of T lymphocyte activation:

Antibody	Dose Concentration (µg/ml)	Inhibition of T lymphocyte activation (% inhibition)
MAb 163.5	80	75
MAb 163.5	70	75
MAb 163.5	50	75
MAb 163.5	25	50

Antibody	Dose Concentration (µg/ml)	Inhibition of T lymphocyte activation (% inhibition)
MAb 253.4	70	85
MAb 253.4	50	85
MAb 253.4	25	50

6. As shown above, the present antibodies to the amino terminal region provide unexpected and enhanced benefits in terms of inhibition of T lymphocyte activation in a manner not disclosed or previously suggested by our prior work. These studies show that relatively low amounts of antibodies can be used to achieve relatively high levels of inhibition of T lymphocyte activation, and such an unexpected

benefit will be useful in the prevention and treatment of the diseases associated with *C. albicans*.

I further declare that all statements made herein are true and correct to the best of my knowledge and that all statements made on information and belief are believed to be true to the best of my knowledge; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated 1/3/05

Margaret K. Hostetter

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